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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,410	12/12/2000	Burkhard Goke	0206-UTL-9	8826

7590 06/30/2005

ARNOLD & PORTER
Attn: IP Docketing Departement, Room 1126B
555 Twelfth Street, NW
Washington, DC 20004-1206

EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,410	GOKE ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-38,41,44-46 and 48-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *44-46 and 48-58* is/are allowed.

6)☒ Claim(s) *10-38 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/11/05, 5/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/27/05 has been entered.

ACKNOWLEDGMENT OF AMENDMENT, REMARKS, IDS STATUS OF THE APPLICATION AND CLAIMS

2. The amendment to the specification, remarks, information disclosure statement and Form PTO-1449 filed 05/27/05 and 04/11/05, respectively are acknowledged, entered and considered. Claims 10-38, 41, 44-46 and 48-58 are now pending in the application. The rejection under 35 U.S.C. 112, first paragraph is withdrawn in view of Applicant's remarks filed 05/27/05.

NEW GROUNDS OF REJECTIONS

CLAIMS REJECTION-35 U.S.C. § 102(b)

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(a) The invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 17, 18, 22-24, 31-38 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Byrne et al (Diabetes, Vol. 46, Supplement 1, page 33A, Abstract # 0127, May 1997).

The abstract of Byrne et al discloses the use of glucagon-like peptide-1 (GLP-1), which improves the ability of the β-cell to sense and response to glucose in subjects with impaired glucose tolerance (IGT). The abstract states that the aim of this study was to establish if GLP-1, a natural enteric peptide and potent insulin secretagogue, improves this defect. Weight matched groups of 5 subjects with impaired glucose tolerance and 5 subjects with non-insulin dependent diabetes (NIDDM) or type II diabetes mellitus were studied on two occasions during a 12 hour oscillatory glucose infusion which meets the limitation of claim 35. The infusion of saline or GLP-1 was at 0.4 pmol/kg/min for 12 hours, (overlap with claimed ranges of claims 22, 23, 33 and 34) wherein the mean plasma glucose (PG) concentrations were significantly lower in both groups during the GLP-1 infusion compared to saline. The abstract concludes by stating that insulin secretion is enhanced in IGT and NIDDM with low dose of GLP-1, but the ability of β-cell to repetitively sense and respond to subtle changes in PG is restored only in subjects with IGT, β-cell dysfunction in IGT is improved by GLP-1 infusion, suggesting that early GLP-1 therapy may delay or prevent the progression of IGT to overt NIDDM. This is a clear indication that the abstract contemplates the

treatment of subjects with IGT whose inability to control glucose had not advanced to the point where those subjects were diagnosed with NIDDM because IGT subjects in the examples had not been diagnosed with NIDDM. Further, if the condition of IGT progresses sufficiently, it can lead to definitive loss of glucose control and to the diagnosis of NIDDM, and as such, would not have been included in the IGT group but instead placed with the NIDDM group. Thus, the abstract clearly provide inherent support for the patient population or the phrase "who has not been diagnosed with NIDDM"

With respect to the limitations wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000 Daltons, the prior art does not disclose the molecular weight of not greater than about 5000 Daltons, however, the abstract discloses the same receptor binding compound, and as such, the molecular weight claimed is an inherent property of the abstract's receptor binding compound. Thus, the prior art meets the limitations of claims 17 and 31. Therefore, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 10, 17, 18, 22-24, 31-38 and 41 as drafted.

CLAIMS REJECTION-35 U.S.C. § 102(a)

4. Claims 10, 17, 18, 22-24, 31-34, 36-38 and 41 are rejected under 35 U.S.C. 102(a) as being anticipated by Byrne et al (Diabetes, Vol. 47, Supplement 1, page A192, Abstract # 0744, May 1998).

The abstract of Byrne et al discloses the use of glucagon-like peptide-1 (GLP-1), which improves first phase insulin secretion without altering insulin sensitivity in subjects with impaired glucose tolerance (IGT). The abstract states that the aim of this study was to establish if GLP-1, a natural enteric peptide and potent insulin secretagogue, improves these defects. Six subjects with impaired glucose tolerance and with early untreated non-insulin dependent diabetes (NIDDM) or type II diabetes mellitus were studied on two occasions during a frequently sampled intravenous glucose tolerance test, with infusion of saline or GLP-1 at 0.4 pmol/kg/min (overlap with claimed ranges of claims 22, 23, 33 and 34) wherein the mean plasma glucose (PG) concentrations were significantly lower in both groups during the GLP-1 infusion compared to saline. The abstract concludes by stating that in subjects with IGT or early-untreated NIDDM; low dose GLP-1 infusion improves first phase insulin secretion in response to an intravenous bolus of glucose. This is a clear indication that the abstract contemplates the treatment of subjects with IGT whose inability to control glucose had not advanced to the point where those subjects were diagnosed with NIDDM because IGT subjects in the examples had not been diagnosed with NIDDM. Further, if the condition of IGT progresses sufficiently, it can lead to definitive loss of glucose control and to the diagnosis of NIDDM, and as such, would not have been included in the IGT group but instead placed with the NIDDM group. Thus, the abstract clearly provide inherent support for the patient population or the phrase "who has not been diagnosed with NIDDM".

With respect to the limitations wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000 Daltons, the prior art does not disclose the molecular weight of not greater than about 5000 Daltons, however, the abstract discloses the same receptor binding compound, and as such, the molecular weight claimed is an inherent property of the abstract's receptor binding compound. Thus, the prior art meets the limitations of claims 17 and 31. Therefore, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 10, 17, 18, 22-24, 31-34, 36-38 and 41 as drafted.

CLAIMS REJECTION-35 U.S.C. § 103(a)

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Byrne et al (Diabetes, Vol. 46, Supplement 1, page 33A, Abstract # 0127, May 1997) taken with WO 98/08531.

The abstract of Byrne et al as discussed above discloses the use of glucagon-like peptide-1 (GLP-1), which improves the ability of the β-cell to sense and response to glucose in subjects with impaired glucose tolerance (IGT). The abstract states that the aim of this study was to establish if GLP-1, a natural enteric peptide and potent insulin secretagogue, improves this defect. Weight matched groups of 5 subjects with impaired glucose tolerance and 5 subjects with non-insulin dependent diabetes (NIDDM) or type II diabetes mellitus were studied on two occasions during a 12 hour oscillatory glucose infusion which meets the limitation of claim 35. The infusion of saline or GLP-1 was at 0.4 pmol/kg/min for 12 hours, (overlap with claimed ranges of claims 22, 23, 33 and 34) wherein the mean plasma glucose (PG) concentrations were significantly lower in both groups during the GLP-1 infusion compared to saline. The abstract concludes by stating that insulin secretion is enhanced in IGT and NIDDM with low dose of GLP-1, but the ability of β-cell to repetitively sense and respond to subtle changes in PG is restored only in subjects with IGT, β-cell dysfunction in IGT is improved by GLP-1 infusion, suggesting that early GLP-1 therapy may delay or prevent the progression of IGT to overt NIDDM. This is a clear indication that the abstract contemplates the treatment of subjects with IGT whose inability to control glucose had not advanced to

the point where those subjects were diagnosed with NIDDM because IGT subjects in the examples had not been diagnosed with NIDDM. Further, if the condition of IGT progresses sufficiently, it can lead to definitive loss of glucose control and to the diagnosis of NIDDM, and as such, would not have been included in the IGT group but instead placed with the NIDDM group. Thus, the abstract clearly provide inherent support for the patient population or the phrase "who has not been diagnosed with NIDDM".

The abstract of Byrne et al differs from claims 1-38 and 41 in failing to teach a) a biologically active analogue of GLP-1 in which combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than ten or five amino acids from the amino acid sequence of GLP-1; b) wherein the receptor binding compound is SEQ ID NO:3 or SEQ ID NO:4; c) wherein the receptor binding compound is expressed by a polynucleotide and wherein the composition further comprises an agent which enhances the half-life *in vivo*; and d) wherein the receptor-binding compound is an organic molecule having a molecular weight of not greater than about 5000 Daltons. However, the reference of WO 98/08531 discloses a composition comprising a compound from the group consisting of GLP-1, GLP-1 analogs, GLP-1 derivatives, and pharmaceutically acceptable salts thereof, at a dose effective to normalize blood glucose by increasing the glucose level in a patient with impaired glucose tolerance (IGT), wherein the GLP-1 is substituted and differs by one or more substitutions, and the amino acid sequences does not differ by more than ten amino acids from the amino acid sequences of GLP-1 and wherein the receptor binding

compound is GLP-1 (See e.g., pages 4 and 7 to 8) as directed to claims 11, 12, 15, 25, 26, and 29, in contrast, to the claimed invention which does not differ by more than five amino acids or ten amino acids from the amino acid sequences of GLP-1. However, given the teachings of WO 98/08531, one of ordinary skill in the art would easily adjust or modify the number of amino acid in a given sequence according to the need because techniques for such replacement, insertion, or deletion are well know in the art to which this invention pertains. Further, on pages 5, 6 and 10, the reference discloses SEQ ID NOS:3 and 4 (i.e., GLP-1 (1-37) and (7-36) amides), which are identical with SEQ ID NOS:1 and 2 of the reference, and as such, meets the limitations of claims 13, 14, 27 and 28.

With respect to the limitations wherein the composition further comprises an agent that enhances the half-life *in vivo* of the compound (claim 19) and wherein the receptor-binding compound is expressed by a polynucleotide (claims 16 and 30). The WO 98/08531 reference clearly shows the preparation of pharmaceutical formulation comprising agents which enhance the half-life *in* vivo of the pharmaceutical formulation including the active agent GLP-1 (e.g., agents used to enhance half-life *in* vivo of the compound are disclosed on pages 16 and 17) as directed to claim 19. The reference also shows the formulation of the amino acid portion of the active compound by methods known in the art, such as recombinant DNA technology, wherein the reference teaches the expression of the receptor binding compound by a polynucleotide (See e.g., pages 11-14 and 16-17) as directed to claims 16 and 30.

On page 18, the WO 98/08531 reference states that administration may be via any route known to be effective by the physician of ordinary skill and cites that parenteral administration is preferred. The reference continues to state that parenteral administration is commonly understood in the medical literature as the injection of a dosage form into the body by sterile syringe or some other mechanical device such as an infusion pump. Parenteral routes include intravenous, intramuscular, subcutaneous, intraperitoneal, etc., and as such meets the limitations of claims 18 and 32. Also, on page 20, the reference discloses the simultaneous administration of the effective amount of the composition in dosage ranges from 0.25 to 6 pmol/kg body weight/min, preferably from about 0.5 to about 1.2 pmol/kg/min, and as such meets the limitations of claims 22, 23, 33 and 34.

Further, in regard to the limitations wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000, none of the prior art disclose the molecular weight of not greater than about 5000, however, both the abstract and the WO 98/08531 reference disclose the same receptor binding compound, and as such, the molecular weight claimed is the expected property of the prior art receptor binding compound. Thus, the prior art meets the limitations of claims 17 and 31.

With respect to the dosage ranges and mode of administrations, the ranges and mode of administrations disclosed in the prior art and claimed by Applicant overlap in scope as discussed above, and as such, the selection of the appropriate dosages and route of administrations would have been *prima* facie obvious because where the

general conditions of claims are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges or situations by routine experimentation.

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at he time the invention was made to employ a method for treating an individual with IGT who has not been diagnosed with NIDDM by administering effective amount of a composition comprising a compound which binds to a receptor of GLP-1, thereby treating IGT. Thus, claims 10-38 and 41 are *prima facie* obvious over the combined teachings of the prior art, absence of sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDANCE

6. Claims 10-38 and 41 are rejected and claims 44-46 and 48-58 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272 0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON WEBER
SUPERVISORY PATENT EXAMINER

/AAM/Mohamed/AAM
June 21, 2005